

# Management of atopy in dogs



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## KEY POINTS

- It is usually not possible to avoid contact with the allergen(s) associated with atopy. The clinical signs must be suppressed with medication.
- The disease may be brought into remission with the use of immunotherapy, although this will require identification of the allergen(s) involved either by enzyme-linked immunoassay (ELISA) testing or intradermal skin testing. About 40% of dogs will respond to immunotherapy and will need little, or no, adjunctive therapy.
- About 50% of atopic dogs will require some degree of steroid therapy – topical, systemic or both.
- Most atopic dogs will benefit from various adjunctive treatments to optimise the cutaneous micro-environment and to minimise the dose of glucocorticoid necessary to maintain remission.

## Introduction

Atopy is a common disease of dogs and accounts for a considerable proportion of the caseload in small animal practice. Dr Nagata covers the detailed aetiology, differential diagnosis and the subtleties of definitive diagnosis of atopy in this issue of *Focus* (see page 4). Immunotherapy, based on identification of relevant allergens is the treatment of choice, and may be expected to have a good effect in some 40–50% cases – particularly in dogs with perennial pruritus. However, this implies that about 50% of atopic dogs will require some other form of symptomatic therapy and, for the vast majority, this will consist of glucocorticoids, in some form or other.

The management of the atopic dog may be considered from two perspectives:

- Adjunctive treatment that will benefit all atopic dogs
- Antipruritic therapy that must be tailored to the individual

## Adjunctive treatment

All animals have a pruritic threshold. When pruritus is perceived to be above the threshold, the animal is pruritic and will scratch. Furthermore, pruritus is additive (**Figure 1**). Thus, atopy plus secondary pyoderma plus otitis externa produces marked discomfort. If, however, the otitis is controlled then the sum of the itch is less and the dog is more comfortable. If the pruritus falls below the pruritic threshold, or if the dog's attention is diverted, it will stop scratching. Adjunctive treatment is utilised to keep the pruritus as close to the pruritic threshold as possible, so that the dose of glucocorticoid, in particular, is minimised.

## Diet

The diagnostic work-up of an atopic dog should include a rigorous dietary exclusion trial of at least six weeks duration, which is specifically designed to screen for dietary sensitivity. All atopic dogs should be fed a commercially



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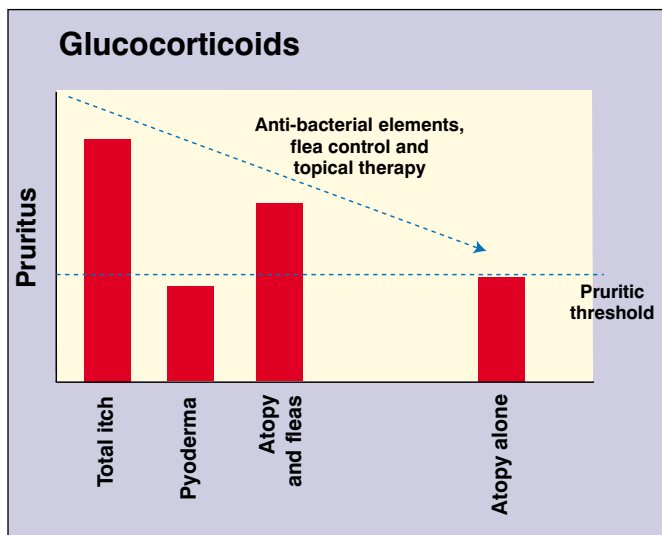
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**Figure 1** Diagrammatical illustration of the concepts of pruritic threshold and summation of itch. All dogs have a pruritic threshold. Thus, in this example, atopy alone is tolerable as the pruritus associated with it is below the pruritic threshold. An atopic with a flea infestation is subject to more pruritus, perhaps sufficient to push the pruritus to the upper limits of tolerance. Superficial pyoderma alone produces some pruritus, again perhaps less than the pruritic threshold. However, if an atopic dog has a flea infestation, and a secondary pyoderma, for example, the total itch is over the pruritic threshold and marked pruritus is seen. Conversely, addressing each cause of pruritus will gradually reduce itch back towards the pruritic threshold.

prepared, nutritionally balanced diet to ensure that cutaneous metabolism is optimal. Normal skin metabolism requires some 30% of the dietary protein intake, in addition to essential fatty acids, amino acids, vitamins and minerals [Lloyd, Marsh. *WALTHAM Focus* 1999 9(2) Optimising skin and coat condition in the dog]. There is some evidence that modifying the diet can affect the dose of glucocorticoid necessary to control pruritus. This is discussed in more detail below.

### Modifying the cutaneous environment

Chronically inflamed skin is oedematous, exhibits an inflammatory infiltrate, possesses poor barrier function (**Figure 2**) and has an increased transepidermal water loss and less surface hydration (1). It is also pruritic. Both topical and systemic therapy may be of value in optimising conditions at the skin surface.

### Shampoo and other topical therapeutics

Cleansing shampoos will remove adhered debris and sweat, and may even alleviate pruritus for a few hours. Topical therapy with humectants and occlusives may help to maintain epidermal hydration by binding water into the stratum corneum (humectant) or occluding the surface and thus inhibiting percutaneous water loss (occlusive). Humectants and moisturisers may also be of benefit after the shampoo therapy, particularly if a drying shampoo, such as benzoyl peroxide, is used (2). Regular use of antimicrobial shampoos will help prevent secondary pyoderma and malassezial dermatitis.

### Dietary therapy

For many years it has been argued that dogs with skin disease often benefit from the addition of 'fat' to the diet. Campbell demonstrated that the addition of sunflower oil (at a dose of 1.5 ml/kg per day) to the diet of dogs with skin disease resulted in a reduction in the concentration of



**Figure 2**  
Poor barrier function associated with chronically inflamed skin.

inflammatory mediators in the epidermis (3). Sunflower oil and polyunsaturated fatty acids (PUFA) may exert their anti-inflammatory effect in one or more of three ways (4, 5):

- By optimising the intercellular lipid layer within the stratum corneum, hence minimising percutaneous water flux and increasing surface hydration.
- By increasing the fluidity of cell membranes, which optimises the function of cellular mediators and receptors.
- By acting as a precursor to anti-inflammatory mediators and antagonising inflammatory mediators.

This last function is more particularly ascribed to PUFA such as linoleic and dihomo-gammalinolenic acids and certain fish oils, which are discussed below. However, if an atopic dog fails to show a positive response to specific PUFA supplementation, it may still be worthwhile adding sunflower oil to the diet, particularly if a dried-type complete diet with a low fat concentration is fed.

One other benefit may derive from fatty acid supplements. Dietary fatty acids become incorporated into epidermal or sebaceous lipids, and if this leads to an increase in the surface concentration of these lipids, it may help to prevent staphylococcal pyoderma. Coagulase-positive staphylococci are more sensitive to EFA than the coagulase-negative members of the normal cutaneous flora.

### Control of ectoparasites

Ectoparasites, particularly fleas, must be rigorously controlled. Atopic dogs are predisposed to develop flea bite hypersensitivity. Furthermore, flea bite hypersensitivity is a cause of pruritus and adds to the overall pruritic load of the atopic dog. Rigorous flea control is mandatory. Any infestation with an ectoparasite (scabies in particular) is likely to provoke a more pruritic response in an atopic dog than in a normal individual because they are already living close to their pruritic threshold. It does not take much to push the pruritus over the threshold.

**Figure 3**  
*Atopic dog with superficial pyoderma.*



### Control of secondary bacterial infection

Changes in surface lipids and altered surface pH favour increased carriage of Staphylococci on atopic lesional skin (6). Increased epidermal permeability facilitates percutaneous passage of bacterial toxins, which further increase cutaneous inflammation [Mason. *WALTHAM Focus* 1997 7(4) Canine superficial pyoderma]. Although dogs maintained on low-dose, alternate-day prednisolone, prednisone or methylprednisolone (PPMP) carry no more Staphylococci on the skin than normal dogs (7), they may still suffer from pyoderma. Indeed, secondary pyoderma is the most common reason for a stable atopic to exhibit increased pruritus (**Figure 3**). This may be difficult to diagnose as systemic glucocorticoids suppress the inflammation associated with pyoderma and the erythematous papules may be hard to detect. Overt bacterial infection should be treated with systemic antibacterial agents and antibacterial shampoos. Regular shampoo regimens will keep the skin clean and reduce the amount of bacterial nutrients on the skin surface.

Dogs treated with long-term, alternate-day PPMP may develop occult cystitis (8). The classic signs of bacterial cystitis (straining, frequent urination) might not be observed because the glucocorticoid reduces the inflammation within the bladder. It has been recommended that dogs treated with long-term PPMP be subject to routine cystocentesis (8), and that the sample is subsequently submitted for bacterial culture and sensitivity testing.

### Control of *Malassezia pachydermatis*

Some dogs carry increased numbers of yeast on their skin [Bond. *WALTHAM Focus* 1997; 7(2) *Malassezia pachydermatis* and canine skin disease] and some atopic dogs carry increased numbers of yeast, compared with normal dogs, although the relationship between the yeast and atopy is not clear. *Malassezia pachydermatis* dermatitis (**Figure 4**) is associated with an intense pruritus, which may not respond well to systemic glucocorticoids. Antimalassezial shampoos (e.g. miconazole, ketoconazole) are usually curative. However some, though not all, dogs may require regular antimalassezial shampoos as part of their regular adjunctive programme.

### Otitis externa and atopy

Chronic, initially ceruminous, otitis externa is commonly associated with atopy (**Figure 5**). A small proportion (often cited as 5%) of dogs with atopy exhibit only uni- or bilateral otitis externa. Many dogs also exhibit hyperplastic lesions on the concave aspects of the pinnae (**Figure 6**). Chronic otitis externa may be associated with otitis media – indeed, it is thought to be the main underlying cause.

Unresolved otitis externa may add considerably to the pruritic load of an atopic dog and should be controlled with appropriate, topical otic medications. Recognising that atopy is the underlying cause of a case of chronic otitis is important, since a simple lateral wall resection is unlikely



**Figure 4**  
*Atopic dog with Malassezia pachydermatis dermatitis.*

to be effective in resolving the problem (**Figure 7**). Vertical canal ablation is more likely to be indicated. Unrecognised underlying allergy (usually atopy) is one of the most common reasons for lateral wall resection to fail, assuming that the objective is to relieve otitis externa.

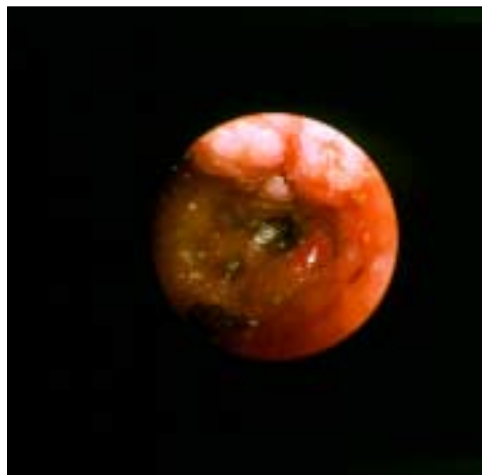
### Antipruritic therapy

#### Specific immunotherapy

Immunotherapy is the treatment of choice for perennially affected dogs. In the order of 40–50%, or more, of atopic dogs might be anticipated to respond well to immunotherapy (9, 10). The protocols for administering the immunotherapy, and the nature of adjuvant and the injection schedule are still a matter of discussion, as no blinded, comparative studies have been performed. Furthermore, there is no clear agreement as to what makes a 'good responder', and this makes comparison of the various publications difficult.

However, if good responders are defined only as those animals that require no supplementary glucocorticoids, then the response rate probably falls to 30–40% at best. Nonetheless, the majority of owners will accept immunotherapy on the basis of a 40% chance of obviating future glucocorticoid therapy.

Immunotherapy is largely free of side-effects and it is economical, cost-



**Figure 5**  
*Otoscope view of early hyperplastic changes within the external ear canal.*

Table 1

**Main causes of steroid-refractory pruritus**

- Scabies
- *Malassezia pachydermatis* dermatitis
- Some cases of food sensitivity
- Mycosis fungoides
- Hepatocutaneous syndrome
- Calcinosis cutis
- Obsessive/psychotic disease (psychodermatoses)

effective (particularly for large dogs) and logistically undemanding for the client. Ideally, dogs will be judged as responding if, after six to eight months of therapy, remission is attained (i.e. no systemic glucocorticoids are required). Some clinicians are happy to accept only a partial response to immunotherapy, judging that a significant reduction in glucocorticoid requirement is better than no reduction at all. It may prove difficult to persuade clients of this, however, and it remains a subjective assessment.

A prerequisite of immunotherapy is identification of allergens, requiring intradermal skin testing or the measurement of circulating IgE titre by *in vitro* means and correlating these with the clinical history. Thus, a history of regular, summer seasonal pruritus would be expected to correlate with demonstrable IgE titres or intradermal sensitivity to grass pollen, for example.

Induction of immunotherapy is achieved by administering a course of injections, usually at monthly intervals, and can take up to six or eight months. During the period of induction it may be necessary to administer low-dose, alternate-day PPMP to control the worst of the pruritus. If remission has not been achieved after nine months of therapy it probably will not occur and symptomatic control will be necessary.

If induction of remission does occur it must be maintained by regular injections of immunotherapy, typically at four-to-eight-week intervals. In many cases, the clients can perform the maintenance injections at home since the volume of injection is constant.

**Symptomatic control of pruritus**

Symptomatic control of pruritus with PPMP, antihistamines or PUFA may be indicated in two clinical situations:

- Control of pruritus pending induction of remission with immunotherapy
- Control of pruritus in the 60% of dogs that fail to achieve remission with immunotherapy and in those cases in which immunotherapy has not been elected

**Glucocorticoids**

Most atopic dogs will respond to long-term, low-dose, alternate-day PPMP at a dose of 0.2–0.5 mg/kg. In some individuals it may be possible to control pruritus with oral PPMP twice a week during the cooler parts of the year.

Initially, dogs may be treated with 0.2–0.5 mg/kg twice daily, for 3–7 days to suppress the pruritus. The dose is then reduced to once daily for a further 3–10 days and then reduced to an alternate-day regimen. In many cases it may be possible to accelerate the switch to the lower dose, and alternate-day medication may be attained within 7–10 days in these animals. Failure to respond adequately should prompt assessment of the diagnosis – is there pyoderma or *Malassezia pachydermatis* dermatitis? The principle differential diagnosis for steroid-refractory pruritus is listed in **Table 1**. Most dogs receiving low-dose, alternate-day, long-term oral PPMP will suffer few side-effects other than transitory polyuria (during induction) and some weight gain, typically 5–10% in medium-sized dogs (authors' observations).

Most owners are able to adjust the dose (and many do so on a regular

**Figure 6**  
*Hyperplastic lesions on the concave aspect of the pinna and the distal region of the external ear canal.*



basis) in order to take account of climatic and management factors that allow for a reduction in dose – for example, active dogs rarely show evidence of pruritus. Conversely, if dogs are subject to periods of inactivity and it is hot and humid, they are more likely to react to the pruritus. This subjective response to pruritus is one reason why many owners report a marked reduction in pruritus when they take their dog on holiday, as increased mental and physical activity results in reduced perception of itch.

Administering PPMP at doses of 0.2–0.5 mg/kg on alternate days is not immunosuppressive and dogs will respond both to annual vaccinations and to immunotherapy. It has been recommended (11, 12) that the alternate-day protocol, in conjunction with the short (< 24 hours) half-life, results in less severe and less rapid onset of iatrogenic hyperadrenocorticism. However, recent work has demonstrated that alternate-day prednisolone (at a dose of 1 mg/kg) does affect the pituitary-adrenal axis, and changes in response to exogenously administered adrenocorticotrophic hormone (ACTH) were demonstrated (12). However, endogenous plasma ACTH concentrations were not significantly different from untreated controls. Thus, alternate-day treatment with PPMP is not without risk, but the severity of adrenal suppression is less severe and the rate of onset is much slower than when it is given on a daily basis.

Some animals are extremely sensitive to even the smallest dose of exogenous glucocorticoid, while others appear almost refractory to side-effects. Each case must be treated on an individual basis. Owners should be aware that even very low doses of PPMP can result in iatrogenic



**Figure 7**  
*Failed lateral wall resection. The dog has atopy and the chronic inflammation of the unresected medial walls of the external ear canal failed to resolve the otitis externa.*

Table 2

**Antihistamines – partial classification, examples and a summary of recommendations**

Class of drug	Example	Dose	Synergy with PUFA?
Ethanolamine	Clemastine	0.05–0.15 mg/kg bid	Yes
Piperazine	Hydroxyzine	2.2 mg/kg tid	Yes
Alkylamine	Chlorphenhydramine	4–8 mg tid	Yes
Phenothiazine	Trimeprazine	0.5–2 mg/kg bid	Yes

Key – PUFA: polyunsaturated fatty acid; bid: q 12 hr; tid: q 8 hr

hyperadrenocorticism. Bi-annual ACTH stimulation tests have been recommended.

If an atopic dog is well controlled and becomes markedly more pruritic, the most likely reason is secondary microbial infection or ectoparasite infestation. Therefore, the dose of glucocorticoid should not be increased. Instead, the animal should be checked for parasites and prescribed an antimicrobial shampoo with systemic antibacterial agents.

**PUFAs**

PUFAs may be successfully used to control pruritus in atopic dogs in a proportion of cases. Clinical studies and double-blind studies with borage seed oil, evening primrose oil and fish oils have consistently demonstrated the beneficial effect of these agents (13, 14, 15). PUFA therapy appears to be dose-responsive. Indeed, it is noteworthy that those studies reporting a good response to PUFA therapy were the studies in which the highest doses of PUFA were given (16).

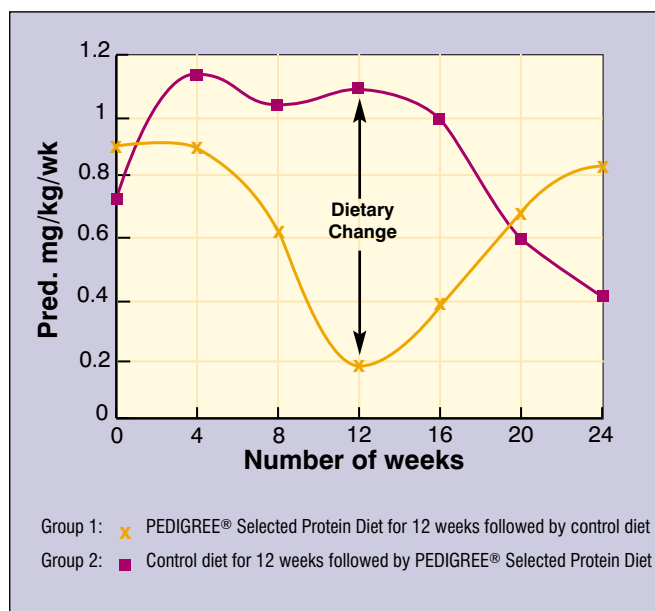
It is not easy to predict which animals will respond, although it is easier to predict that those with secondary infection or severe cutaneous inflammation will not. Thus, every effort must be made to suppress infection and provide a 'clean playing field' before they are used. This may necessitate a few weeks of PPMP if the skin is chronically inflamed. Frequently, there is a lag period before EFAs exert their maximum effect. Although the duration of this period is variable, it is prudent to allow a period of at least two months to elapse before judging that there is no response to the supplement. Thus, owners and clinicians should be cautioned not to expect dramatic results. Concurrent use of one or several antihistamines may reveal synergistic effects in some dogs (17), as described below. Similarly, the use of EFAs in conjunction with PPMP may allow for a reduction in the dose of glucocorticoid necessary to control the pruritus.

**Antihistamines**

The use of antihistamines to control atopy in dogs is continually being re-evaluated. Undoubtedly, one of the principle reasons for their poor reputation is the fact that there are as many as eight different chemical groups of antihistamines. Failure with one does not necessarily imply that none will be effective and the clinician is advised to try several – at least one from each class. Clemastine, chlorpheniramine and hydroxyzine are probably the most useful (17, 18). Furthermore, some antihistamines appear to demonstrate synergistic effects with PUFAs and glucocorticoids (19), as shown in **Table 2**. Thus, with patience, it may be possible to find a regimen combining PUFAs with antihistamines that effectively suppresses the pruritus, alleviating the requirement for PPMP.

**Strategies to reduce the dose of glucocorticoid**

Most dogs with atopy express modest to marked pruritus, which varies from day to day. However, the pruritus does not usually interfere with normal activity. Thus, they do not scratch all night, they rarely scratch during exercise and they do not scratch in the consulting room. Individual



**Figure 8** The effect of diet on dose of glucocorticoid necessary to control atopy. Mean weekly prednisolone dose in 12 atopic dogs fed one of two diets.

variation may be marked, which is why management must be tailored to the individual. This variation in pruritus is one reason why PPMP on an alternate-day basis is so successful. It enables owners to react quickly to factors that may allow for a reduction in dose, or, conversely, enables them to increase the dose for short periods, thus preventing serious relapse.

Once the pruritus is more or less under control and the dose of PPMP is more or less constant, it is possible to assess whether supplementary EFA or antihistamine allows for a further reduction. In some cases a significant sparing of the necessary dose of PPMP may be achieved, even in cases where control with the EFA or antihistamine alone or in combination was not adequate.

In addition to PUFA supplementation, other dietary factors may be important adjuncts to therapy, potentially sparing the requirement for corticosteroids. This was illustrated in a clinical study conducted in atopic dogs using a commercial canned diet with protein sources limited to chicken and rice (20). Twelve perennially affected atopic dogs maintained in clinical remission on oral, alternate-day, low-dose prednisolone therapy were entered into a six-month, open, crossover study (20). The dose of prednisolone had been kept largely stable and the dogs had been maintained on a variety of commercial diets for the two months prior to the study period. None of the dogs had shown any improvement during a three-week trial with a home-prepared, restricted diet of chicken, rice and water. The dogs were randomly assigned to one of two groups, and fed either PEDIGREE® Selected Protein Diet (chicken and rice), or a control diet that was a canned food based mainly on fish, maize and wheat. Each diet was fed for three months before crossover, when the diets were reversed. Dogs were evaluated every four weeks for the dose of prednisolone required to control their clinical signs and for clinical score of pruritus, erythema, interdigital oedema, alopecia, self-trauma and coat condition. The prednisolone dose and the total clinical score were significantly ( $p < 0.05$ ) reduced when PEDIGREE® Selected Protein Diet was fed to the dogs, compared with when the control diet was fed (**Figure 8**). The nutrient(s), or raw materials, responsible for these differences were not identified in this study, and therefore further studies are needed. Nevertheless, these data indicate that diet – particularly a limited protein source and a relatively high-fat diet – can have a marked impact on the management of canine atopy, as measured

by changes in the dose of anti-inflammatory drugs required to maintain remission of clinical signs. Therefore, switching to a diet of this type should be considered as a further form of adjunctive therapy.

## Summary

There is good evidence to suggest that atopic dogs do better, require less steroids, and suffer fewer complications if under the care of a dermatologist (9). This is partly because dermatologists deal with referred cases where owner motivation is good and partly because they understand the complexities of the disease and the secondary complications. There is no reason why primary care clinicians should not obtain equally good results (as measured by prescribing minimal doses of glucocorticoid) given client motivation, good communication and a clear vision of what can be achieved.

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